NEUROLOGY AND EUGENICS

The Role of Experimental Genetics in their Development

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THE neurologist, who is so often helpless to check the development of insane or criminal tendencies, is naturally interested in the theoretical possibility of modifying the expression of undesirable genotypes, and is therefore led into making genetical experiments with that object. The first part of this article deals with such experiments.

As long as genetical research was mainly concerned, as it was until recently, with discovering the mechanism of gene transmission, it dealt with the genes which we can call 'strong'—those, that is, which cause the expected ratios to appear, and which equally affect all individuals. But there is also a second type of gene, a 'weak' type, which we find, with variable frequency, in plants and animals, and of which no doubt there are many in man. The weakness is characterized by the fact that some individuals carrying this type of gene go through their whole lives without manifesting the character, a phenomenon which is described in German as a lower *Penetranz** of the gene involved. Morgan's analysis has shown that *abnormal abdomen* of *Drosophila melanogaster* is a character of this type, since its transmission is according to mendelian laws, though it is only apparent in a certain percentage of the individuals carrying the gene. If that gene were one for some illness or criminal tendency, only a proportion of the carriers would exhibit it—the rest being healthy or normal—while all of them would transmit it according to the appropriate mendelian expectation.†

Doubtless many of the diseases of the central nervous system which appear 'sporadically' (i.e. in proportions which fit no known mendelian ratio) in certain families are caused by such 'weak' genes. My collaborator Patzig, for instance, has published an account of monozygotic twins, now 43 years old, one of whom manifested in youth a hereditary predisposition to dementia praecox, while the other has remained sane.‡

Recent experiments of Gabritschewsky, as well as earlier work of my colleagues N. W. and H. A. Timoféeff-Ressovsky, have shown that it is possible to modify the *Penetranz* of a gene by environmental factors, one of which is nutrition. Gabritschewsky found that in a well-nourished culture of the *giant* mutant (*Drosophila melanogaster*) 90 per cent. were giants, though there were only 10 per cent. in a badly fed culture. We can see from these studies that there may be a possibility of influencing gene manifestation by chemical means.

EFFECT OF ONE GENE ON ANOTHER

The manifestation of a gene may also be differentially affected by the 'remainder genotype,' by the influence, that is, of the complex of all the other genes. In Gabritschewsky's work the effectiveness of the same *giant* mutation varied in cultures of different 'remainder genotypes'—40 per cent. *giant* in one culture and 70 per cent. in another. Further, N. W. Timoféeff examined in *Drosophila funebris* the mutation

* There is no English equivalent for this word, but the description should make its meaning clear.

† The reference, of course, is not to an ordinary recessive character.

‡ Perhaps, however, this remarkable instance is due to the asymmetry mechanism which causes somatic segregation in identical twins. See the studies of Professor H. H. Newman, and especially the notice of his recent work on page 66 of this REVIEW.—ED.

venae transversae incompletae (*Xvti*), a gene which causes an interruption or failure of the cross veins in the wings. In most cultures this gene mutation is only manifest in a few individuals; but if it is crossed with a culture of flies showing another gene mutation *radius incompletus* (*ri*: shortening of the second longitudinal vein of the wing) its *Penetranz* may rise to 100 per cent.

In this case one gene profoundly affects the manifestation of another. We may perhaps expect in the future to employ this type of mechanism for eugenic purposes, though our present knowledge of human genotypes is inadequate, and, even if it were not, it would still be difficult to choose the appropriate combination of genotypes for this or that purpose.

Another phenomenon to be observed in 'weak' genes is a tendency to be more markedly manifest in some individuals than in others.* Though perhaps of less significance, this is surely not unimportant to eugenics. N. W. Timoféeff has shown that variations in the degree to which a gene manifests itself are something other than variations in *Penetranz*. He has proved that lower *Penetranz* may be combined with an increased degree of manifestation in both *ri* and *Xvti*. The character, that is, may appear in fewer than usual of its carriers, though in some of them it will be more than ordinarily strongly marked. The decreased *Expressivität* of a disease or of an anti-social tendency would be manifested in a milder form of the complaint or in a weaker tendency to anti-social actions.

According to the same worker, the degree of manifestation may be modified both by the 'remainder genotype' and by environmental factors; and the eugenic attitude towards the phenomenon must therefore be the same as that towards the phenomena of *Penetranz* in genes.

A third type of 'weak' gene is that which lacks specificity and which may therefore manifest itself in more than one way. In particular, a type of 'specificity' which may later be of eugenic importance, is what we may call 'polar specificity.' Genes of this type can cause deviations from the normal in either a positive or a negative direction, and they may provide an explanation of the fact—if fact it be—that highly gifted and subnormal (or mentally unbalanced) personalities occur in the same family. The fact, however, has not yet been substantiated, though the subject, under some such intriguing title as "Genius and Insanity," is a popular one for somewhat uncritical discussions. Our experience at this Institute seems to indicate that the 'remainder genotype' can, again, affect the numbers of positive or negative variants.

DIFFERENT EFFECTS ON VITALITY

I would call attention, too, to a further set of experiments by N. W. Timoféeff, who had been testing different mutations as to their vitality. When he crossed two such strains of low vitality—different mutants, that is, but each with reduced viability—he usually found that the viability of the offspring was even lower than that of either parent stock, the reduced vitality of one mutation being added to that of the other. But in some cases the contrary occurred, each mutant apparently compensating for the defects of the other, with the result that the vitality of the offspring was greater than that of either parent stock. Eugenics must therefore reckon with the possibility that the crossing of two genotypes may in some cases balance certain disturbances of the inner organs, although the exterior characteristics of both genes are manifested together in the hybrids.

There is one further point of eugenic importance, best illustrated by such a disease as Huntington's chorea. If one parent is heterozygous for this complaint, which is due to a dominant gene, 50 per cent. of the offspring will inherit the predisposition and, since the *Penetranz* of the gene amounts to 100 per cent., will sooner or later succumb to the disease. Since, however, its onset may be delayed for many years, it is

* In German this is described as a variable *Expressivität*, which might perhaps be translated as a variable 'potency.'—ED.

very important for both eugenic and therapeutic reasons, to distinguish, as early as possible, between these children who are inevitably doomed to the disease and the remaining 50 per cent. of the family who are entirely free from it. Experimental genetics has indeed shown that such a hereditary predisposition may be associated with certain other characters, the so-called 'stigmata.' Pearl observed, for instance, that the recessive gene mutation in Drosophila *vestigial* (wings) is always accompanied by reduced vitality when it is homozygous, but that the vitality of the heterozygous carriers of it is unaffected; and N. W. Timoféeff found exactly the same when studying the mutation *miniature* in *Drosophila funebris*.

By the aid of stigmata, therefore, it may sometimes be possible to recognize in advance those individuals who carry the hereditary predisposition to a disease. C. Vogt, indeed, has already pointed out that the skulls of sufferers from Huntington's chorea are very often unusually small, while Meggendorfer found that children with the predisposition can at an early stage be distinguished from the normal by their psychopathic character.

It can be seen from the foregoing that experimental genetics may throw light on eugenic problems, as well as on those of general heredity, and by materially assisting the study of the diseases of the central nervous system (and, indeed, of other complaints) may sooner or later be of practical use in eugenics.

GENETICS AND THE BRAIN

Having now indicated some of the ways in which experimental genetics can assist neurology, we will turn to those questions which the eugenist would gladly see answered by the neurologist. Above all, what sort of brain is socially valuable?

The brain consists of an unexpectedly large number of kinds of nerve cells which differ morphologically and physiologically from each other, and which together constitute the physical basis of mental activity. Since the size of the brain does not allow of the unlimited development of all kinds of cells, the hypertrophy of some groups must be accompanied by the hypo-trophy of others; and the function of neurology is to discover precisely how each different combination is reflected in the mental abilities of the individual. What combinations, in particular, of groups of cells provide the basis of socially valuable qualities, and why is it that those qualities, when possessed by only one of the parents, are, as we all know, so seldom transmitted to the children? The reason is that a marked talent of this type, being the immediate product of a certain individual combination of nerve cells, is fundamentally due to another and very complex combination of genes which is almost inevitably broken up in the reduction division at oogenesis or spermatogenesis. The very process of breeding shatters the peculiar combination which creates the talent.

The problem of positive eugenics is therefore how to conserve such gifts.

There may be less loss when marriages occur between men and women with similar talents; and certain circus families can show a conservation of their particular gifts over several generations, because each husband and wife have been similarly talented workers at the same craft. The same phenomenon can be seen in some families of artists. The social trend of to-day, which eugenics should support, favours this sort of conservation of talent, since the increase of women in industry tends to encourage marriages between people with kindred gifts.

EUGENICS AND BIOLOGICAL HARMONY

Finally, surely eugenics should not be concerned only with mental qualities, but should aim at fostering harmonies of genes, and at the same time take into account the highly relevant fact that some genes have manifold effects ('polytopic manifestation').

We know, for instance, that a single gene mutation in a wild species of Drosophila may lower the vitality of the organism. The probable explanation of this is that the occurrence of the mutation automatically

creates a new genotype, a new combination of genes which is less well balanced and therefore less well adapted to the environment than was the old genotype whose harmony of genes produced strong and resistant individuals.

A disturbance of this harmony, leading to an impairment of viability, may be accompanied by external changes which are not themselves the cause of the impairment —like, for instance, the larger number of head-bristles in Drosophila, a mutation which is accompanied by a loss of vitality. The gene fundamentally responsible for these associated changes must have a ' polytopic ' effect, not only causing the alteration in the external character, but also disorganizing the harmonious development of the internal organs. It is impossible to tell beforehand whether the gene for some valuable mental quality may not have unfavourable effects on other organs; and eugenic wisdom must therefore regard the general physiology and metabolism of the human being, instead of merely concentrating upon some special mental gifts.